PRÊMIO JOSÉ RIBEIRO DO VALLE – 2025

O prêmio José Ribeiro do Valle, oferecido a cada ano pela SBFTE, visa identificar a cada ano os melhores trabalhos científicos desenvolvidos por jovens investigadores na área da Farmacologia. Entre os trabalhos inscritos para esta vigésima sétima edição do prêmio, foram selecionados cinco finalistas, que fizeram apresentações de seus respectivos trabalhos perante comissão julgadora, em sessão pública durante o 57º Congresso Brasileiro de Farmacologia e Terapêutica Experimental, realizado de 21 a 24 de outubro de 2025 no Complexo CDI e Inova da Universidade de São Paulo (USP). O resultado foi o seguinte:

Primeiro prêmio

Julia Sapienza Passos

- 10.014 **Multifunctional Thermosensitive Nanocarriers for Local Treatment of Non-Invasive Breast Cancer: Tissue Localization, Cytotoxic and Molecular Effects**. Passos JS[1,2], Machado-Neto JA[1], Panitch A[1], Lopes LB[1] [1]ICB-USP, Department of Pharmacology, Functional and Molecular Biology Program, Brazil; [2]Georgia Institute of Technology, Department of Biomedical Engineering, USA

  Breast cancer remains a major cause of mortality among women and a clinical challenge due to its heterogeneity and resistance to current therapies. Standard therapy typically includes surgery, radiotherapy, hormone therapy, and chemotherapy. However, less invasive approaches—such as intraductal drug delivery—offer promising alternatives for managing pre-tumor lesions and non-invasive forms of the disease, such as ductal carcinoma *in situ* (DCIS). This route enables localized drug delivery and reduces systemic toxicity, although technical limitations persist. In this scenario, nanosystems can help to achieve the full benefits of the route by improving tissue retention, selectivity and cytotoxicity. In this study, nanostructured lipid carriers (NLC) were developed and evaluated for paclitaxel (PTX) intraductal delivery. They presented size <600 nm, encapsulation efficiency >90% and stability. To improve tissue retention and add thermosensitive properties (i.e., responsiveness to biological temperature), two modifications were explored. In one, NLCs were dispersed in Poloxamer 407 to form *in situ* gels; in the other, they were coated with the thermosensitive polymer poly(N-isopropylacrylamide) (PNIPAM) to obtain hybrid nanoparticles (NP-H) functionalized with type I collagen-binding peptide (SILY), which is overexpressed in the mammary tumor microenvironment. Incorporating NLCs into the gel prolonged retention of hydrophilic (2.2–3.0-fold) and lipophilic (2.1–2.3-fold) fluorescent probes in mammary tissue *in vivo* compared to unmodified NLCs or probe solutions. PNIPAM coating increased NLC size by 140 nm and prolonged drug release for up to 120 hours in response to biological temperature. Functionalization with SILY promoted adhesion to collagen secreted by MCF-7 and T-47D breast cancer cells. Drug cytotoxicity in MCF-7 and T-47D 3D spheroids increased upon treatment with nanoparticles compared to the solution, although IC_{50} values varied according to the type of nanoparticle: NLC (59.0–80.3 μM) > NP-H (90.6–116.5 μM). PTX-loaded NP-H functionalized with SILY showed selectivity evidenced by lower cytotoxicity towards non-tumor

(MCF-10A) cells. PTX-loaded NLC and NP-H induced apoptosis and microtubule stabilization in MCF-7 and MDA-MB-231 cells, as evidenced by PARP-1, BAX, and acetylated α-tubulin expression, along with disrupted microtubule organization in the cytoskeleton. Notably, NP-H also increased γH2AX expression, indicating DNA damage and suggesting that nanoencapsulation alters PTX's mechanism of action. Unlike PTX solution, NP-H showed no vascular effects on the chorioallantoic membrane of fertilized eggs, yet effectively inhibited angiogenesis, reducing vessel growth by 6.1–7.8-fold. These results underscore the importance of thoughtful nanoparticle design to enhance therapeutic properties and enable novel targeted strategies for breast cancer treatment. **Financial support:** FAPESP 2018/13877-1, 2020/01208-8, 2021/12664-7, 2023/12246-6 and CAPES – Brazilian Federal Agency for Support and Evaluation of Graduate Education within the Ministry of Education of Brazil (finance code 001)

Segundo prêmio

Carolina Medina Coeli da Cunha

- 04.068 **Tyrosine Kinase Inhibitor Reduces Systemic and Cerebral Inflammation in Experimental Sepsis**. Cunha CMCD[1,2,3], Moraes BPT[1,3,4], Abreu VHP[1,3], Soares GVM[1,3], Moraes-de-Souza IM[1,2,3], Almeida MAP[1], Estato V[1], Sayão PGF[1,3,4], Souto HA[1,3], Bozza PT[1,2], Castro-Faria-Neto HC[1,2], Silva AR[1,2], Gonçalves-de-Albuquerque CF[1,2,3,4] [1]IOC-Fiocruz, Immunopharmacology Lab, Rio de Janeiro, Brazil.[2]IOC-Fiocruz Postgraduate Program in Cellular and Molecular Biology, Rio de Janeiro, Brazil. [3]Unirio, Immunopharmacology Lab, Rio de Janeiro, Brazil. [4]Unirio, Postgraduate Program in Molecular and Cellular Biology, Rio de Janeiro, Brazil

  Introduction: Sepsis is a leading cause of death worldwide (1). Its pathophysiology involves dysregulated inflammation, increased inflammatory mediators, increased leukocyte infiltration, vascular changes, and neuronal impairments (2). Sepsis-associated encephalopathy affects around 70% of septic patients and contributes to a worse prognosis (3). Src family kinases (SFKs) are a family of protein kinases involved in regulating chemotaxis, cell adhesion and migration, cytokine secretion, and endothelial permeability. Inhibition of SFK attenuates exacerbated leukocyte and endothelial responses in inflammatory reactions (4-7). Bosutinib is a multiple kinase inhibitor clinically used in the treatment of chronic myeloid leukemia with a potent effect on SFK (8). This study investigates the potential of bosutinib as a treatment for sepsis. **Methods:** Swiss mice were divided into 4 groups: Sham+Bosutinib; Sham+Vehicle; Cecal Ligation and Puncture (CLP)+Bosutinib, and CLP+Vehicle. CLP was used to induce a polymicrobial sepsis model. Treatments were administered orally 30 minutes before and 6 hours after surgery with bosutinib (3 mg/kg) or vehicle. Survival analysis was performed for 7 days, and clinical score assessment was performed 24 hours after surgery. Also 24 hours later, peritoneal lavage (PL), plasma, and brain were collected. Intravital microscopy was performed to assess leukocyte-endothelial adhesion, capillary density, and cerebral blood perfusion. Cytokines and chemokines were measured by enzyme-linked immunosorbent assay in PL, plasma, and brain tissue. PL were cultured to analyze the growth of colony-forming units, the total and differential leukocyte count was performed on these samples. All experimental procedures were approved by the Animal Use Ethics Committee of IOC (L015/2015; L026/2022) and UNIRIO (2019/03). Results and **Conclusion:** Bosutinib improved clinical scores and survival in sepsis, reduced sepsis-induced cytokine levels in PL, plasma, and brain tissue. It reduced leukocyte recruitment, mainly neutrophils, and bacterial growth in the PL of CLP animals. Bosutinib treatment also improved capillary density and blood perfusion, and reduced

leukocyte recruitment and adhesion in the cerebral microcirculation of septic mice. These results demonstrate that bosutinib modulates leukocyte recruitment and attenuates systemic and cerebral dysregulated inflammation and neurovascular alterations in experimental sepsis. Funding: FAPERJ, UNIRIO, CNPq, CAPES (Grant 001), IOC, FIOCRUZ, BCM.

Menção Honrosa

Mariana Burille Moretti

- 07.010 **Probenecid Potentiates the Relaxant Effect of β-Adrenergic Agonists in the Prostate of Rats**. Moretti MB, Leonardi GR, Barros JVC, Lima JM, Monica FZ Unicamp, PPG Pharmacology, Brazil

Luiz Adriano Damasceno de Queiroz

- 04.030 **Aging, Immunity and Metabolism: Divergent Effects of Rapamycin in Senescence-Prone and -Resistant Mice**. Queiroz LAD[1], Barros RS[1], Assis JB[2], Pantoja KC[1], Bustia SX[1], Sá-Nunes A[2], Rodrigues SFP[3], Turato WM[4], Silva CCC[5], Migliorini S[1], Martins JO[1] [1]USP, FCF, Dept. of Clinical and Toxicological Analyses, Lab. of Immunoendocrinology, Brazil; [2]USP, ICB, Dept. of Immunology, Lab. of Experimental Immunology, Brazil; [3]USP, ICB, Dept. of Pharmacology, Lab. of Vascular Nanopharmacology, Brazil; [4]USP, IQ, Dept. of Biochemistry, Energy Metabolism Lab., Brazil; [5]USP, FCF, Dept. of Clinical and Toxicological Analyses, Multi-user Preclinical Imaging Center, Brazil

Brena Freire de Oliveira Claudino

- 08.002 **Prevention of Gut Microbiota Imbalance: The Role of** *Arthrospira platensis* **in Hypercaloric Diet-Induced Dysbiosis**. Claudino BFO[1,2], Arruda RRA[1,2], Diniz AFA[1,2], Melo MB[1], Sousa-Filho JEC[1], Colunga AAG[4], Nobre CSN[4], Silva BA[1,2,3] [1]UFPB, Lab of Functional Pharmacology Prof. George Thomas, Institute of Research in Drugs and Medicines, Brazil [2]UFPB, Postgraduate Program in Bioactive Natural and Synthetic Products, Health Sciences Center, Brazil [3]UFPB, Department of Pharmaceutical Sciences, Health Sciences Center, Brazil [4]University of Minho, Fermentations Lab, Centre of Biological Engineering, Portugal

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